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Cavernous Transformation of the Portal Vein in a Child With Non-Hodgkin's Lymphoma

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We present an 11 year old boy who developed collateral vessels in the portal hepatis with non-visualization of the portal vein 9 months after treatment for large cell lymphoma. This ''cavernous transformation of the portal vein'' may lead to varices with subsequent gastrointestinal hemorrhage. Med. Pediatr. Oncol. 29:143–145, 1997. © 1997 Wiley-Liss, Inc.

Key words: non-Hodgkin's lymphoma; portal vein obstruction; cavernous transformation

INTRODUCTION

Cavernous transformation of the portal vein is the formation of venous collateral vessels in the hepatoduodenal ligament [1]. These collateral veins are formed from enlarged pancreaticoduodenal and biliary veins [2], and occur most frequently after obstruction of the extrahepatic portion of the portal vein. Cavernous transformation of the portal vein is almost invariably found with secondary splenomegaly [3]. The diagnosis consists of visualization of multiple small vessels within the porta hepatis with concurrent absence of flow in the portal vein itself [4,5].

In this report we present a patient with non-Hodgkin's lymphoma who developed cavernous transformation of the portal vein 9 months after presentation. Cavernous transformation of the portal vein has not been reported to be associated with lymphoma nor with its treatment.

CASE REPORT

While receiving chemotherapy for an abdominal non-Hodgkin's lymphoma an 11-year-old boy was found by routine follow-up computed tomographic (CT) scan of the abdomen to have splenomegaly.

The patient had been well until 8 months earlier, when a 3.3 × 3 cm ulcerated skin lesion was noted in his right lateral flank. Microscopic examination of skin biopsy showed lymphohistiocytic and granulomatous lesions with ulceration. No malignant cell infiltrate was seen. Two months after the biopsy he complained of headaches, decreased appetite, fever, progressive weakness, night sweats, and weight loss. Radiographs of his chest were normal. Further follow-up examination 2 months later revealed persistence of the symptoms, a 20 lb weight loss, and cervical adenopathy. A lymph node biopsy was obtained, and histologic examination showed non-specific acute and chronic inflammatory changes. Just prior to the referral to our institution, 8 months after the first symptoms, the patient became jaundiced and massive retroperitoneal adenopathy was noted.

On physical examination at our institution the patient appeared thin and ill with generalized icterus. The patient's growth and development were appropriate for his age. His temperature was 37.4°C, his pulse rate was 123/min, and his respiratory rate was 22/min. His blood pressure was 134/85 mmHg.

The hematocrit was 25%, the white blood cell count was 26,300 cells/mm^3 (82% neutrophils, 6% lymphocytes, 7% monocytes, 2% eosinophils, and 3% band forms), the platelet count was 385,000/mm^3, and the erythrocyte sedimentation rate was 55 mm/hr. The prothrombin time was 13.9 sec (control 10.8 sec), partial thromboplastin time was 27.9 sec (control 29.5 sec), thrombin time was 13 sec (control 13.7 sec), and the fibrinogen concentration was 452 mg/dl. The glucose level was 109 mg/dl, and the serum protein concentration was 6.3 g/dl (albumin 3.2 g/dl, globulin 3.1 g/dl). The aspartate aminotransferase level was 259 U/l, the alanine aminotransferase concentration was 187 U/l, total bilirubin was 3.9 mg/dl (direct bilirubin 3.4 mg/dl), the alkaline phosphatase level was 722 U/l, and the serum lactate dehydrogenase concentration was 985 U/l (normal range 340–770 U/l). Microscopic examination of stained bone marrow films and of bone marrow biopsy specimens revealed no tumor. CT revealed a large retroperitoneal,

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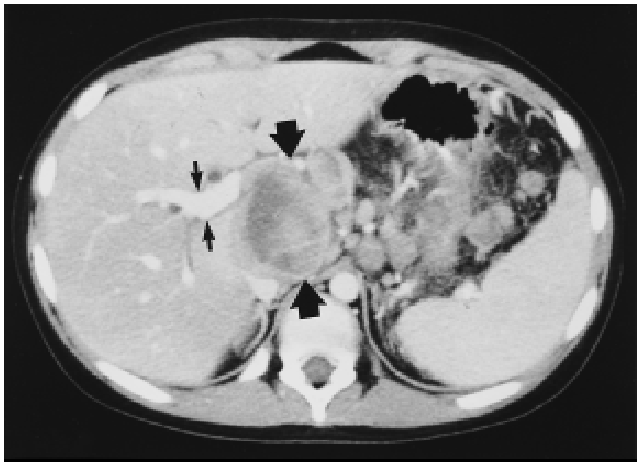

Fig. 1. An axial CT image of the abdomen demonstrates a large mass in the porta hepatis (large arrows). Portal venous flow is maintained (small arrows).

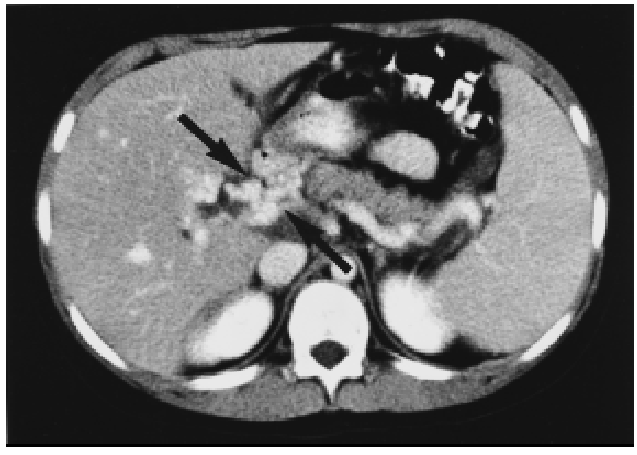

Fig. 2. An axial CT image of the abdomen at follow-up reveals multiple serpiginous vessels in the porta hepatis (arrows). The main portal vein is not seen. Ascites was present in the lower abdomen and pelvis but is not seen on this image. There is splenomegaly.

upper abdominal mass in the porta hepatis, with central necrosis and abdominal ascites (Fig. 1). A gallium-67 citrate scan demonstrated avid accumulation of radiopharmaceutical in the superior mediastinal and right iliac regions. Technetium-99m methylene diphosphate (MDP) skeletal imaging revealed no increased uptake of the radiopharmaceutical in the bones. The patient was admitted and an exploratory laparoscopy was performed. A large mass in the porta hepatis was seen. Multiple biopsies with a Trucut needle were obtained, and peritoneal washings were submitted for analysis. Histologic examination of the mass revealed non-Hodgkin's lymphoma of the anaplastic large cell histiotype and T-cell immunophenotype. Microscopic examination of a sample of cerebrospinal fluid revealed no tumor cells. The patient was enrolled on our institutional protocol for non-Hodgkin's lymphoma and achieved a clinical and radiologic complete remission. The patient received 2 courses of ''DAC'' which consists of dexamethasone (40 mg/m^2/day, 4 days), cytarabine (2 g/m^2, q 12 hr, 2 doses), and carboplatinum by intravenous continuous infusion (at a dose of 540 mg/m^2). On day 43, he received cyclophosphamide (800 mg/m^2, intravenous, 1 dose), adriamycin (75 mg/m^2, intravenous, 1 dose), vincristine (1.5 mg/m^2 [maximum 2 mg], intravenous, 1 dose), and dexamethasone (12 mg/m^2/day, 14 days). As consolidation, he received vincristine (1.5 mg/m^2 [maximum 2 mg], intravenous, day 1), adriamycin (75 mg/m^2, intravenous, day 1), 6-mercaptopurine (225 mg/m^2, p.o., days 1–5), and L-asparaginase (10,000/m^2, intramuscular, 3 times/week, 6 doses). Maintenance chemotherapy consisted of 3 courses of combination chemotherapy: 1) DAC; 2) vincristine (1.5 mg/m^2 [maximum 2 mg], intravenous, day 1), 6-mercaptopurine (225 mg/m^2, p.o., days 1–5), methotrexate (60 mg/m^2, intravenous, day 1), and dexamethasone (40 mg/m^2/day, 5 days); and 3) vincristine (1.5 mg/m^2 [maximum 2 mg], intravenous, 1 dose), cyclophosphamide (800 mg/m^2, intravenous, 1 dose), adriamycin (30 mg/m^2, intravenous, 1 dose), and dexamethasone (40 mg/m^2/day, 5 days). Granulocyte colony stimulating factor was used after each course of DAC. Each chemotherapy course was started when the absolute neutrophil count was >300/mm^3 and platelet count was >100,000/mm^3. No central nervous system-directed therapy was administered. The patient tolerated the chemotherapy well. After 9 months, at the off-therapy date, CT of his abdomen revealed cavernous transformation of the portal vein with associated mild splenomegaly (Fig. 2). Follow-up CT examinations 1 year later again demonstrated cavernous transformation of the portal vein without evidence of recurrent lymphoma.

DISCUSSION

The most common cause of extrahepatic portal vein obstruction in the pediatric age group is thrombosis. In addition, portal vein obstruction may be idiopathic [2,4] or result from congenital atresia of the portal vein [6]. In neonates, portal vein thrombosis with subsequent cavernous transformation has been seen after septic omphalitis or catheterization of the umbilical vein [5]. This obstruction has been found in older children after blunt trauma to the abdomen [4,7] or splenectomy [8].

Cavernous transformation of the portal vein has been rarely associated with malignancies in adults [9,10]. One case of cavernous transformation of the portal vein has been reported in a child with hepatocellular carcinoma [11]. Portal venous thrombosis in these cases generally results from direct portal venous invasion by tumor cells, notably hepatocellular carcinoma. In non-metastatic gas-

tric carcinoma, tumor cells invade vessels at the primary site and subsequently extend into the main portal vein and cause portal tumor thrombi [10]. This mechanism is also associated with cavernous transformation of the portal vein in cases of myelofibrosis [12]. We can only speculate on the precise etiology of the portal vein obstruction that leads to cavernous transformation in our patient. He did not receive L-asparaginase, which is widely known to produce thrombosis. Although a tumor in the porta hepatis could obstruct the portal vein by mass effect alone, this would be an unlikely explanation for our patient's obstruction because his tumor bulk decreased in response to therapy. Non-Hodgkin's lymphoma usually does not invade vessels, although some anaplastic large cell lymphomas have involved vascular structures. In those cases, the tumor cells formed cuffs around vessels and appeared to blend into the myxoid matrix, leading to vascular destruction and necrosis [13]. Particularly in non-Hodgkin's lymphoma of the large cell histiotype the clinical manifestations can be heterogeneous and misleading. Moreover, lymphoma cells have been shown to produce interleukin (IL)-1, IL-4, IL-6, IL-8, tumor necrosis factor, and granulocyte colony stimulating factor; these cytokines are believed to be important in the pathogenesis of the disease and may be involved in the recruitment of neutrophils, monocytes, fibroblasts, and endothelial cells [14]. In our patient, perhaps the invasion of the portal vein by lymphoma was followed by a local inflammatory reaction, resulting in portal vein fibrosis that persisted despite regression of the tumor. In response to the resulting obstruction of the portal vein, the typically minute periportal venous collateral vessels enlarged leading to the serpentine collateral vessels seen in the porta hepatis on the follow-up CT.

Patients with cavernous transformation of the portal vein eventually form esophageal, gastric, and duodenal varices [5], although blood flow within the cavernous vessels usually remains hepatopetal. Most patients remain undiagnosed until they present with rupture of a varix [6]. Up to 80% of these children will have gastrointestinal bleeding [7,15]. Identification of cavernous transformation of the portal vein is important because it facilitates detection of varices and their timely treatment with surgical portosystemic shunts or sclerotherapy. We recommend follow-up imaging by CT of the abdomen every 6 months in patients with non-Hodgkin's lymphoma who have cavernous transformation of the portal vein.

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